US Army Medical Research and Materiel

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Prophylactic and Therapeutic Monoclonal Antibodies

Features and advantages:

- **Could use individual MAbs or mixtures to detect, prevent or treat alphavirus infections**
- **MAb 13D4 protected mice from death after challenge with virulent VEE virus**
- **Could use for *in vitro* detection of alphaviruses that have and have not cleaved E3-specific MAbs**

Patent Status

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This invention is a method for producing prophylactic and therapeutic monoclonal antibodies (MAbs) which recognize glycoproteins found on alphaviruses. Alpha-viruses include the Venezuelan equine encephalitis (VEE) virus, which causes an incapacitating febrile illness in humans. All alphaviruses contain two envelope glycoprotein spikes, E1 and E2, which function during attachment of the virus to a cell. Three E1:E2 heterodimers associate to form one VEE virus glycoprotein spike. Normally the precursor to E2 (PE2) is cleaved to form E2 and E3.

The MAbs were generated from V3526, a site-directed mutagenic VEE laboratory strain which has a deletion of the PE2 glycoprotein cleavage site and a suppressor mutation. Six of the MAbs protected mice from a lethal VEE virus challenge. One MAb, 13D4, protected BALB/c inbred mice from death after challenge with virulent VEE virus when at least 20 μg of 13D4 was administered to the mice prior to challenge. Although the other five MAbs protected fewer than half of the mice, they did significantly extend the mean time of death.

The reactivity of the MAbs was shown applicable against a broad variety of wild type and laboratory alphavirus strains, using *in vitro* ELISA, western blot, immunoprecipitation, and plaque reduction neutralization tests. The generation of murine MAbs to a previously unknown protective epitope after vaccination suggests V3526, is an improvement in VEE vaccine development. As the new vaccine candidate continuously exposes E3 to the immune system, it is likely to be more effective than current PE2 cleaving vaccine strains at eliciting protective antibodies.

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